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Lens-free Microscopy Using Acoustically Actuated Nanolenses and its Applications

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Abstract: Integration of acoustically actuated nanolenses into a lens-free microscopy enables a cost-effective platform for detection of nanoparticles and nanoliter volume rheology. We demonstrate the detection of single nanoparticles and the rheological analysis of viscoelastic fluids. © 2019 The Author(s)

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1. Introduction

Nanoparticles are widely used for biosensing applications including labels for immunoassays and DNA detection [1]. However, the sensitivity of these assays is limited to the challenges associated with detecting single nanoparticles in liquid samples. Classical methods for their characterization include the scanning electron microscopy, atomic force microscopy, dynamic light scattering and super-resolution microscopy are not effective due to small field-of-view, high-cost and the need for bulky equipment and complex sample preparation steps. Most critically, the specimen has to be in a dry state, limiting their use in point-of-care applications. Recent advances in electronics and computational power has enabled field portable detection of nanoparticles using lens-free microscopy. Self-assembled or vapour condensed nanolenses have further improved the detection limit for this technique [2], although in these cases, the sample has to be in a dry state. In contrast, acoustic waves are known to easily couple and propagate in different materials media, including liquids [3]. We show that integration of acoustic waves with lens-free microscopy has overcome many of the the aforementioned limitations, opening up new applications in biosensing. Since acoustic wave propagation is dependent on the material medium, we demonstrate monitoring the wave propagation provides valuable information regarding local rheological properties [4].

2. Methods

Our detection system combines computational photonics with ultrasonic wave propagation in order to develop new methods for nanoparticle detection and rheological characterization of liquids. The device comprised through-transmission lens-free microscope constructed using light emitting diodes that are butt-couple to individual optical fibers, a band-pass filter, an interdigitated transducer (IDT) and a complementary metal oxide (CMOS) imaging chip. The sample was placed on a disposable chip in a thin liquid layer and coupled to the IDT. The IDT generated a surface wave of 9.74 MHz on a lithium niobate crystal which, upon interaction with the disposable glass chip (145 μm), propagated as a dispersive Lamb-type wave, caused deformations of the thin liquid layer above. The finite geometry and an impedance mismatch caused the Lamb-type wave to reflect back from the glass-air boundary, hence created a standing wave. These standing acoustic waves resulted in mechanical deformation of the waveguide (the solid-liquid bilayer). We observed that this deformation of the liquid had a lens-like convex meniscus which acted as nanolenses' around nanoparticles, enhancing their optical signature and enabled their detection on a low-cost CMOS imaging chip.

3. Results and Discussion

We characterized the system with commercially sourced polystyrene spherical nanoparticles of different sizes (140 nm - 1000 nm), and demonstrated its application in biosensing using herpes simplex virus (HSV-I) (150 nm

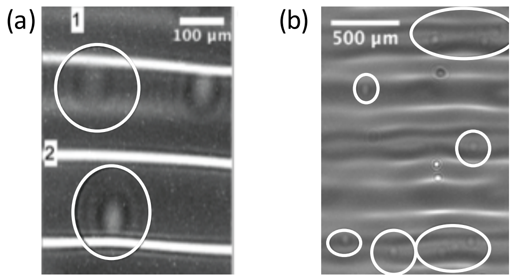

Fig. 1. (a) Lens-free image of 250 nm polystyrene particles, and (b) Herpes simplex virus type 1 (150 nm - 200 nm) in polyethylene glycol (PEG400) on a disposable chip.

- 200 nm) and Staphylococcus aureus bacteria (800 nm - 1000 nm) samples. Figure 1 shows the detected 250 nm biotinylated polystyrene nanoparticles and HSV-I on a glass biochip in polyethylene glycol (PEG400).

Experimental results on characterizing local rheological properties show that relaxation of a liquid film deformed by an acoustic wave is dependent upon the physical properties of the sample. We used this phenomena to study the viscosity of different water-glycerol mixtures. Figure 2 shows that these measured relaxation times are inversely proportional to kinetic viscosity of the liquid, enabling rheological characterization of nanoliter samples.

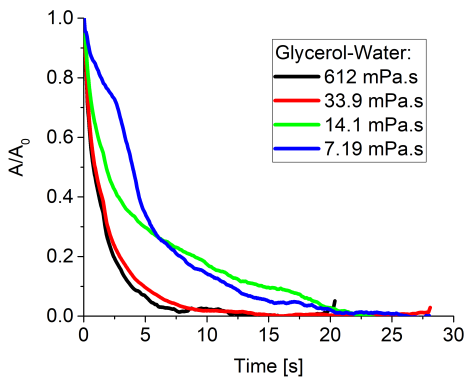

Fig. 2. Experimental transient response of the relaxation of various glycerol-water mixtures.

4. Conclusion

By using computational photonics coupled with an understanding of acoustic wave propagation in liquid, we have demonstrated the ability to detect nanoparticles in samples using a wide field-of-view ($\sim$30 mm^2), low-cost, high-throughput for portable lens-free microscopy. Furthermore, the method enables the study of the rheological properties of nanoliter liquid samples. Our method can be readily integrated into different types of biosensing strategies, enabling high-throughput detection of nanoparticles, viruses and bacterial cells with simultaneous rheology measurements in liquids.

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